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other insects to treated surfaces (*13*). An effort is being made to select the most logical approach to a standard evaluation of such surface treatments (*8*).

The commercial popularity of aerosol insecticides has likewise brought about a demand for a standard test method as a means of evaluating the performance of aerosol bombs. Most methods now in use simply require a test room in which to apply the aerosol against actively flying insects.

BIOLOGICAL ASSAY

Still another objective of insecticide testing is biological assay as a supplement to chemical analysis. Such assays have been proposed for the gamma isomer of benzene hexachloride, and have been utilized as a check on chemical results in the study of the nature of tetraethylpyrophosphate.

CONTROL OF VARIABLES

Other variables than the species of insect may be inherent in the insect or they may be a matter of environment. Related to the organism are the stage of the insect with respect to life cycle, age within each stage, weight, and sex—all factors which can affect profoundly the results of controlled tests. Environmental factors of greatest importance are temperature, moisture or humidity, and quality and quantity of food. A thorough understanding of insect biology is therefore necessary for the most effective work in testing insecticides.

Although the nonbiologist is likely to overlook the importance of variation in the insects used for test purposes, the biologist frequently underrates his ability to control the variables in biological test material. The precision of individual assays is greater when the homogeneity of the test population is increased and as the procedure is further standardized. The degree to which control of variation in test insects and method should be attempted depends upon the refinement which results warrant. Increased control requires more time and equipment. It increases the quality of results at the expense of quantity. On the other hand, it provides more reliable data with fewer tests involving smaller numbers of organisms.

LITERATURE CITED

(1) Anon., *Soap Sanit. Chemicals*, Blue Book, pp. 207–10, 1947.
(2) Bottimer, L. J., *Soap Sanit. Chemicals*, **21** (12), 151–9 (1945).
(3) Campbell, F. L., and Filmer, R. S., *4th Internat. Congr. Entomol., Trans. II* (1928), 523–33 (1929).
(4) Carpenter, E. L., and Moore, Wm., *J. Econ. Entomol.*, 31, 270–5 (1938).
(5) Cotton, R. T., *Pub. Am. Assoc. Advancement Sci.*, 20, 144–51 (1943).
(6) David, W. A. L., *Bull. Entomol. Research*, **36**, 373–93 (1946).
(7) David, W. A. L., *Nature*, **155** (3929), 204 (1945).
(8) Doner, M. W., *Soap Sanit. Chemicals*, **23** (6), 139–43, 193 (1947).
(9) Hansberry, Roy, *Pub. Am. Assoc. Advancement Sci.*, 20, 85–94 (1943).
(10) Hansberry, Roy, Middlekauff, W. W., and Norton, L. B., *J. Econ. Entomol.* **33**, 511–17 (1940).
(11) McGovran, E. R., and Fales, J. H., U. S. Dept. Agr., Bur. Entomol. Plant Quarantine, *Circ.* **ET-239** (1947).
(12) McGovran, E. R., and Mayer, E. L., *Ibid.*, **ET-208** (1943).
(13) Monro, H. A. U., Beaulieu, A. A., and Delisle, R., *Soap Sanit. Chemicals*, **23** (8), 123–9, 143–5 (1947).
(14) O'Kane, W. C., Glover, L. C., and Blickle, R. L., New Hampshire Agr. Expt. Sta., *Tech. Bull.* **76** (1941).
(15) O'Kane, W. C., Walker, G. L., Guy, H. G., and Smith, O. J., *Ibid.*, **54** (1933).
(16) Pearson, A. M., and Richardson, C. H., *J. Econ. Entomol.*, **26**, 486–93 (1933).
(17) Peet, C. H., and Grady, A. G., *Ibid.* **21**, 612–17 (1928).
(18) Richardson, C. H., *Pub. Am. Assoc. Advancement Sci.*, **20**, 126–35 (1943).
(19) Richardson, C. H., and Seiferle, E. J., *J. Econ. Entomol.*, **32**, 297–300 (1939).
(20) Shepard, H. H., Lindgren, D. L., and Thomas, E. L., Univ. Minnesota Agr. Expt. Sta., *Tech. Bull.* **120** (1937).
(21) Siegler, E. H., and Munger, Francis, *J. Econ. Entomol.*, **26**, 438–45 (1933).
(22) Siegler, E. H., Munger, Francis, and Gahan, J. B., *Ibid.* **27**, 1140–2 (1934).
(23) Swingle, M. C., *Pub. Am. Assoc. Advancement Sci.*, **20**, 82–4 (1943).
(24) Swingle, M. C., Phillips, A. M., and Gahan, J. B., *J. Econ. Entomol.*, **34**, 95–9 (1941).

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Use of DDT Insecticides on Food Products

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Because small amounts of DDT in animal food cause the storage of large amounts in animal products which are used in enormous quantities by man, the question of the safety of DDT on and in food products becomes critically important. Experiments with rats fed DDT over a period of 2 years are discussed.

THE general availability and effectiveness of DDT as an insecticide introduce the possibility of its widespread occurrence in food products. The most serious source of danger from the use of DDT is the repeated ingestion of small amounts that cling to forage, fruits, and vegetables that have been treated with this insecticide. The possibilities of acute poisoning in man from the consumption of food products sprayed with DDT are so limited that incidences of acute intoxication can be expected to occur only from gross carelessness.

Damage to the livers of animals fed repeated doses of DDT has been observed extensively in laboratory animals (*2, 4, 5*). This damage usually consists of hypertrophy of the centrolobular hepatic cells, increased oxyphilia of their cytoplasm with a slight hyaline appearance, and peripheral segregation, basophilia, and increased size of the hepatic cell cytoplasmic granules. In the more marked examples on higher-dosage schedules, there are focal hepatic cell necrosis and distortion of lobular architecture. The livers of chronically fed rats are enlarged as much as 60% and slices from these livers studied by standard Warburg procedure show a 40% decrease in oxygen utilization (*3*). The level of DDT intake which shows histopathological lesions in animals is much below that which shows significant gross effects such as retardation of growth and hyperexcitability. The author has observed slight damage to the livers of rats on levels of DDT in the diet as low as 10 p.p.m. However, no gross effects have occurred in rats fed less than 400 p.p.m. DDT.

The pathological lesions observed have revealed wide individual variations in susceptibility to poisoning in a given animal species. Nevertheless, the type of lesion has been consistent throughout the different species.

The storage of DDT in the tissues, especially in the fatty

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tissues of animals ingesting small amounts, has been demonstrated in cows, monkeys, dogs, rats, rabbits, and poultry (*7–9, 11*). DDT has been shown to be secreted in the milk of cows, goats, dogs, and rats (*8, 9, 11*). Other animals fed the milk from the DDT-treated animals showed toxic symptoms. All the DDT in the milk appears to be concentrated in the butterfat portion and to be transferred to the butter (*6*); therefore, a relatively small amount of DDT in the whole milk results in a significant amount in the butter. The quantities of DDT that are stored apparently depend both on the level of ingestion and on the length of time over which the intake occurs. With low dosage levels, it has been shown in rats that a maximum storage level appears to be reached in about 2 months. However, with higher dosage levels there is continual storage of additional DDT (*10*). In long term experiments dosage levels of DDT from 10 to 200 p.p.m. in the diet produce relatively similar amounts of DDT in the fat (Table I). An animal may store amounts equivalent to several acute intravenous lethal doses without showing any obvious signs of intoxication. The accumulation of appreciable quantities of DDT in animal tissues at low dietary levels (all levels appear to produce storage in fat) poses a difficult problem, since many animal products are used for human consumption. This may be especially important in the case of infants, whose chief food is milk. The presence of small amounts of DDT in animal food, therefore, assumes the same importance as relatively larger amounts on fruits and vegetables consumed directly by man.

Table I. DDT Content of Perirenal Fat of Individual Rats Following Ingestion of DDT for 2 Years

DDT Content of Diet, P.P.M.	DDT Content of Perirenal Fat, P.P.M.
10	119
10	270
100	103
100	129
200	313
200	158
400	1091
400	966
800	4220

The withdrawal of food from animals on high dosage levels of DDT produces characteristic DDT tremors. This effect occurs both in starvation experiments with DDT-treated animals and in DDT-treated animals made sick by an infection (*2*). In the latter case the animals supposedly were metabolizing their body fat containing the DDT in the same manner as a starved animal. This effect could be important in cases of human illness where there is an appreciable storage of DDT in the body.

After the cessation of exposure to DDT, fat storage in rats is reduced in 15 to 30 days to a negligible level (*1*). Furthermore, livers of animals fed DDT recover rapidly and show a normal appearance in 8 to 10 weeks (*2*).

Reproduction studies in progress in this laboratory show that 50 p.p.m. DDT in the diet reduces the number of young rats that live through the nursing period (Table II). DDT in a concentration as high as 600 p.p.m. in the diet did not affect the number of living young at birth in the first generation. However, in the second generation there were very few living young at birth in the group on 600 p.p.m. DDT and none of these lived through the nursing period. No effect on reproduction has occurred with 10 p.p.m. DDT.

Table II. Effect of DDT on Reproduction in Rats

	Dosage Level, P.P.M. in Diet				
	600	100	50	10	0
No. of litters	8	7	8	10	9
No. of living young at birth	58	64	57	72	58
Average weight at birth, grams	5.8	5.9	5.8	5.9	6.0
Young weaned, %	31.0	59.4	63.2	87.5	88.0

CONCLUSIONS

Significant amounts of DDT are stored in the body tissues of animals, especially in adipose tissues, at levels in the diet as low as 10 p.p.m.

Histopathological lesions occur in the livers of rats fed 10 p.p.m. DDT in their diet for 2 years.

Individual susceptibility to the toxic effects of DDT varies markedly within any given species.

Gross effects such as retardation of growth and hyperexcitability do not occur in animals at the low levels of DDT intake which produce significant liver damage.

Relatively high dosages of DDT in the diet markedly affect reproduction in rats. Dosage levels of 50 p.p.m. DDT reduce the number of weanling rats.

LITERATURE CITED

(1) Draise, J. H., and Woodard, G., *Actualities Medico-Chirurgicales*, No. 12, 5 (1946).
(2) Fitzhugh, O. G., and Nelson, A. A., *J. Pharmacol.*, **89**, 18 (1947).
(3) Laug, E. P., and Fitzhugh, O. G., *Ibid.*, **87**, 18 (1946).
(4) Lillie, R. D., and Smith, M. I., *Pub. Health Repts.*, **59**, 979 (1944).
(5) Nelson, A. A., Draise, J. H., Woodard, G., Fitzhugh, O. G., Smith, R. B., Jr., and Calvery, H. O., *Ibid.*, **59**, 1009 (1944).
(6) Schechter, M. S., Haller, H. L., and Pogorelskin, M. A., *Agr. Chemicals*, **1**, 27 (1946).
(7) Telford, H. S., *Soap Sanit. Chemicals*, **21**, 161 (1945).
(8) Telford, H. S., and Guthrie, J. E., *Science*, **102**, 647 (1945).
(9) Wilson, H. F., Allen, N. N., Bohstedt, G., Betheil, J., and Lardy, H. A., *J. Econ. Entomol.*, **39**, 802 (1946).
(10) Woodard, G., and Ofner, R. R., Federation Am. Soc. for Exptl. Biol., *Federation Proc.*, **5**, 215 (1946).
(11) Woodard, G., Ofner, R. R., and Montgomery, C. M., *Science*, **102**, 177 (1945).

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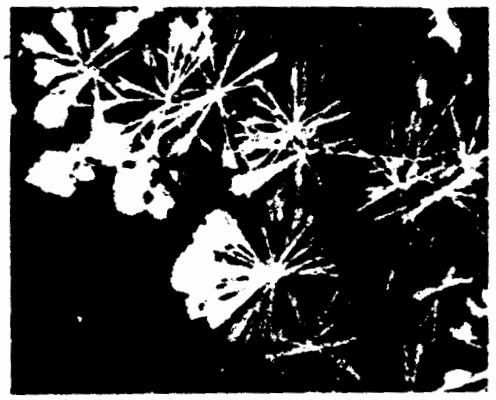

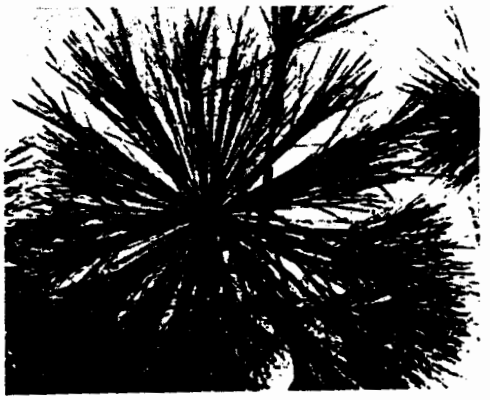

Crystals of Pure DDT

Magnified about 69 times (*left*), magnified about 260 times (*right*)